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Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building, 1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the HPV Test Plan for Tris (4-t-butyl-3-hydroxy-2,6-dimethyl)-s-triazine-2,4,6-(1H,3H,5H)-trione

Dear Administrator Leavitt:

The following comments on Cytec's test plan for the chemical Tris (4-t-butyl-3-hydroxy-2,6-dimethyl)-s-triazine-2,4,6-(1H,3H,5H)-trione are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

Cytec Industries, Inc. submitted its test plan on September 9, 2003, for the chemical Tris (4-t-butyl-3-hydroxy-2,6-dimethyl)-s-triazine-2,4,6-(1H,3H,5H)-trione (CAS No. 40601-76-1), commercially known as CYANOX 1790 Antioxidant. This substance is used as an antioxidant in food packaging materials and polymer systems such as polystyrene and polyethylene. A number of ecotoxicity and mammalian toxicity studies have been conducted with Tris (4-t-butyl-3-hydroxy-2,6-dimethyl)-s-triazine-2,4,6-(1H,3H,5H)-trione. Cytec has compiled existing data and has utilized structure activity relationship programs and models to estimate physicochemical properties and environmental fate for this chemical. We commend this approach for assessing hazard and exposure risk for HPV chemicals; the EPA has also encouraged the use of this method (EPA, 2002).

At this time, however, we question Cytec's assessment that a combined reproductive/developmental toxicity test (OECD 421) is needed to meet the requirements of the HPV program. If conducted, this test will result in the death of at least 675 animals.

We are concerned that little attempt has been made to bridge the data gap for developmental toxicity with existing data from similar or analogous chemicals. Cytec lists chemical names synonymous with Tris (4-t-butyl-3-hydroxy-2,6-dimethyl)-s-triazine-2,4,6-(1H,3H,5H)-trione in its test plan but the CAS numbers for these chemicals differ from the sponsored chemical. Specifically, Cytec identifies 1,3,5-triazine-2,4,6

(1H,3H,5H)-trione as a synonym for the sponsored chemical but with a CAS number of 108-80-5, rather than 40601-76-1. We are unclear as to whether 1,3,5-triazine-2,4,6 (1H,3H,5H)-trione, also known as cyanuric acid, is the same chemical as Tris (4-t-butyl-3-hydroxy-2,6-dimethyl)-s-triazine-2,4,6-(1H,3H,5H)-trione or a similar chemical. Furthermore, the multiple trade names given in the test plan are confusing (CYANOX 1790 Antioxidant, CYANOX 1790, CYNOMIX 1790); are these the same chemical as CYANOX?

We are also concerned that Cytec overlooked two existing studies on reproductive/developmental toxicity endpoints for the chemical 1,3,5-triazine-2,4,6 (1H,3H,5H)-trione (CAS No. 108-80-5). One study published by the EPA showed no dominant lethal response in studies of teratogenic and reproductive effects of cyanuric acid in mice and rats (EPA, 1981). Another study showed no significant differences in implantation and resorption sites, embryos, or mutation rates between test and control groups after dosing of monosodium cyanurate (CAS No. 108-80-5) (Clayton *et al*., 1982). We also located teratological studies on CYANOX in rats (Yamamoto *et al*., 1972) that could be used to satisfy the SIDS endpoint for developmental toxicity for Tris (4-t-butyl-3-hydroxy-2,6-dimethyl)-s-triazine-2,4,6-(1H,3H,5H)-trione, once its relationship to the sponsored chemical is explained. We strongly urge Cytec to review these studies in order to avoid separate and/or duplicative testing for the developmental toxicity endpoint. It may well be that by considering several "older" studies into one weight-of-evidence overview, these data may be sufficient to meet this SIDS endpoint, especially for a screening level program.

Duplicative studies violate the basic tenets of animal welfare and the HPV program. In keeping with animal welfare principles set forth by the EPA, including EPA's stated goal that HPV participants "maximize the use of existing and scientifically adequate data to minimize further testing" (Wayland, 1999), the EPA should ask Cytec to examine all existing data before deciding whether to conduct its own developmental tests. Without this analysis, it is otherwise completely unwarranted to conduct further, unreliable animal tests, which would kill many animals and only serve as a "check-the-box" exercise.

We are hopeful that Cytec will reconsider their proposal to kill 675 animals in a reproductive/developmental toxicity that may be completely redundant. Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 327, or via e-mail at *meven@pcrm.org*.

Sincerely,

Megha Even, M.S.
Research Analyst

References

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